Remarks

Applicant respectfully notes that the claims of invention V, *i.e.*, claims 12-17, are currently pending, following the election in the response of April 14, 2008. Applicants have amended claims 12 and 13 to recite to "S6 kinase 1 inhibitors" instead of "S6 kinase modulators". Support is found in the patent application as filed, paragraph bridging pages 4-5. No new matter is added.

With the amendment, none of the claims recite non-elected subject matter. Accordingly, the claims objections have been obviated.

Obviousness-type double patenting rejection

The Examiner has rejected claims 12-16 as allegedly unpatentable over claims 13-17 of U.S. patent application 10/568,637. Applicants respond that this rejection of claims 12-17 is a provisional rejection, since the allegedly conflicting claims have not yet been allowed. Should it become necessary as prosecution progresses, Applicants would consider obviating this objection by filing a terminal disclaimer.

§112 first paragraph rejection

The Examiner has rejected claims 12-16 for alleged lack of enablement and for insufficient written description. The Examiner alleges that the specification does not desribe or enable a method that prevents any weight disorder by using any agent that affects any S6 kinase activity. Applicants respectfully traverse.

The invention relates to a method of using S6 kinase 1 inhibitors in a new indication for a known target. S6 kinase 1 is already known in the art and suggested as a potential target, in cancer and angiogenesis (see page 3, lines 1-2 of the patent specification). S6 kinase 1 inhibitors were also known in the art at the time of filing (see page 3, lines 2-5 reciting examples of S6 kinase 1 inhibitors). The patent specification provides clear guidance to identify other S6 kinase 1 inhibitors without undue burden.

The scope of the method is limited. The S6 kinase activity is defined in the new claim as S6 kinase 1 activity. The agent is functionally characterized as an agent inhibiting S6 kinase 1 activity. Weight disorder is defined specifically in the claims as related to a disorder dependent on fat accumulation.

The Examiner goes on to allege a lack of teaching of a successful method, and questions regarding tolerance to modification of the steps and reagents used in a successful method. However, the present invention is based upon the finding that S6K1 deficient mice show a severe reduction in white fat and brown fat due to a reduction in a fat cell size and that S6K1-/- mice are protected against fat accumulation, due to a sharp increase in basal lipolysis and a highly elevated metabolic rate. The correlation between S6K1 activity is not only shown

using knockout mice having no S6K1 activity (Examples 1-8) but also shown with (i) adipose tissue data from obese and normal mice tissue and (ii) obesity model mice with elevated S6K1 activity (see Example 9).

This correlation between fat accumulation and S6 kinase 1 activity would indicate to one of skill in the art that inhibitors of S6 kinase 1 would find use in *e.g.*, diagnosis or treatment of any disorders resulting in fat accumulation. The claimed use has been asserted by *in vivo* data in animal model, and the claimed use could only be further evaluated in a clinical trial. An applicant for a patent is not required to provide results from human clinical trials.

In view of the teaching and data presented in the specification, the present specification adequately discloses and enables the claimed methods of treatment. Applicants respectfully request that this rejection be withdrawn.

§103 rejection

The Examiner rejected Claims 12 and 13 as being unpatentable over published PCT patent application WO 00/66721 ("*Bjorbaeck*") in view of Diggle *et al*, *Biochem. J.* 316(Pt 2): 447-453 (June 1, 1996) and Damoiseaux *et al.*, *Transplantation* 62:994-1001 (October 15, 1996). Applicants respectfully traverse.

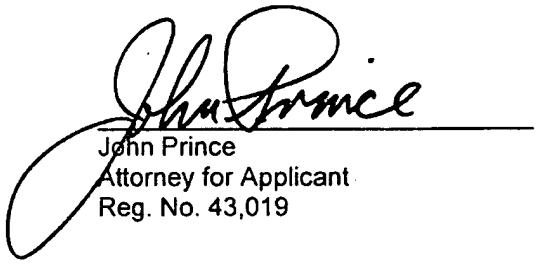
The claimed invention is related to inhibition of S6 kinase 1 (also called S6K1; p70/p85S6K). By contrast, *Bjorbaeck* discloses that the deletion of the *rsk2* gene (ribosomal-S6-kinase (p90rsk)) in mice results in reduced body weight, reduced body fat and reduced sensitivity to diet-induced weight gain, as well as lower levels of leptin in the serum of *rsk2* deficient mice as compared to wild type littermates. S6 kinase 1 and RSK2 are distinct proteins. *Bjorbaeck* does not teach or suggest to a person skilled in the art that S6 Kinase 1 can be used as target to screen and identify agents effective in treating or diagnoses of weight disorders. *Bjorbaeck* exclusively relates to the use of RSK2 as target to identify or screen for agents effective in reducing body weight or body fat or in treating obesity.

Furthermore, the two proteins are not activated by the same pathway. S6 kinase 1 activation occurs via mTOR (mammalian target of rapamycin. S6 kinase 1 is part of a pathway which is inhibited by rapamycin as disclosed for example by *Diggle*. By contrast, RSK2 is part of the Ras-dependent MAPK cascade (see *e.g.*, *Bjorbaeck*, page 1, lines 11-24) and is directly phosphorylated and activated by ERK1 and ERK2. For further details please see also the introduction of Edelmann *et al., J. Biol. Chem.* 271(2):963-71 (January 12, 1996), a copy of which is provided in the Supplemental IDS. .

Therefore, the one skilled in the art would not have derived from *Bjorbaeck* any teaching regarding the role of S6K1 in fat accumulation and would have had no motivation to test known S6 kinase 1 inhibitors for treating or prevent weight disorders dependent upon fat accumulation. Thus, the claimed invention is not obvious over the cited references. Applicants respectfully request that this rejection be withdrawn.

An early and favorable action on the merits is respectfully requested. Should the Examiner have any questions, please contact the undersigned attorney.

Respectfully submitted,



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